CLAIMS

What is claimed is:

1. A process for the preparation of sidechain-bearing cephalotaxane of the following formula and/or a salt thereof

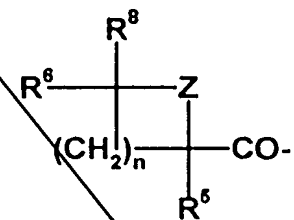
Ω-CO-O-CTX

where

Ω ("omega") is a representative radical of the chain terminal moiety and -CO- is the carbonyl of the ester group bonded to cephalotaxane;

the Ω-CO- radical is corresponding:

- either to the following substituted heterocycloalkane formula:



where n is included between 0 and 8;

Z is oxygen, nitrogen or sulfur heteroatom;

R^5, R^6 and R^8 are independently

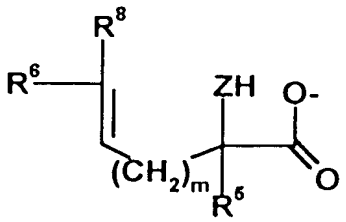
hydrogen;

hydrocarbon radical, saturated, insaturated or aromatic, linear or ramified and/or cyclic, especially alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heterocycloalkyl, of said radical including or not heteroatom(s); R^6 and R^8 may be included in a cycle ;

oxygen ether bearing one of the former radicals;

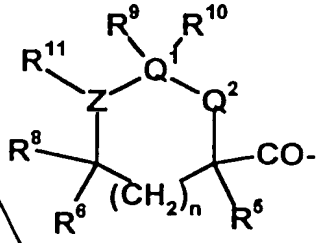
- or to the following linear alkene formula:

Sub a' 7 cont.



where m is included between 1 and 8;
R^5, R^6 and R^8 are as defined above;

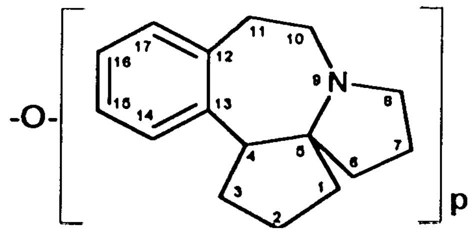
- or to the following formula:



where n, R^5, R^6 and R^8 are as defined above;
Z and Q^2 are independently oxygen, nitrogen or sulfur heteroatom;
Q1 is carbon, silicium or phosphorus atom;
R^9 and R^{10} are independently hydrogen, alkoxy, hydrocarbon radical, including or not heteroatom(s), saturated, unsaturated or aromatic, linear or ramified and/or cyclic, especially alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heterocycloalkyl;
R^9 and/or R^{10} having the ability to be null or taken together to make an heteroatom and/or make a multiple bond with Q^1, R^9 and R^{11} having the ability to be null to make a multiple bond between the two atoms of carbon bearing them; and
R^{11} is hydrogen, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl or alkylcarbonyl;

where

-O-CTX is cephalotaxine moiety of the following formula a salt thereof:

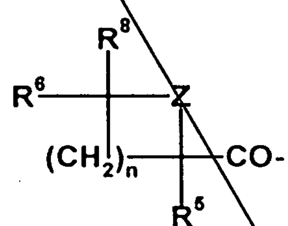


where p is equal to 1 or 2;

the two types of radicals -Ω and –CTX above-mentioned being bonded with an ester bond –CO-O-

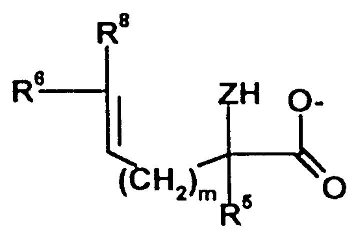
the said process bringing together:

- either carboxylic acid with general formula Ω-CO-OH or a salt thereof;
- or an activated form of an acid with general formula Ω-CO-A or a salt thereof, with Ω-CO of the following formula:



where n, Z, R^5, R^6 and R^8 are as defined above;

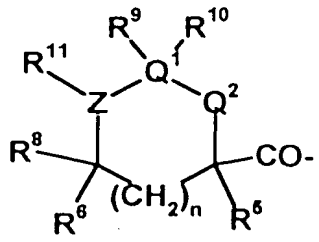
where Ω-CO of the following formula:



m is included between 1 and 8, Z, R^5, R^6 and R^8 are as defined above;

where Ω-CO of the following formula:

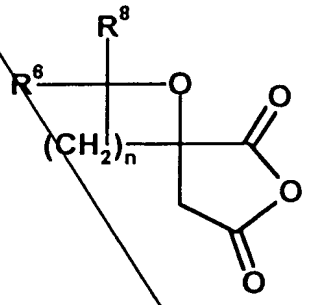
Sub. 7 a' cont.



where n, Z, Q^1, Q^2, R^5, R^6, R^8, R^9, R^{10} and R^{11} are as defined above

A represents:

- either cyclic anhydride of the following formula:



where n, R^6 and R^8 are as defined above;

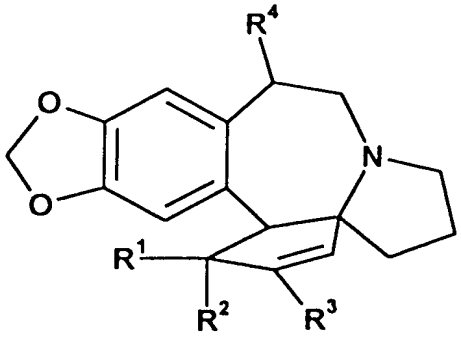
this reaction has been completed by methylation of the primary carboxyl thus formed, with:

- either a hydroxyl group bearing cephalotaxane or a salt thereof of the formula H-O-CTX, where CTX are as defined above;
- or a metallic alcoxide of the formula M-O-CTX, where CTX are as defined above and M is a metal;
-or an activated form of its hydroxyl group of the formula Y-O-CTX, where –O-CTX is as defined above and Y is, either a leaving group to allow a negative charge on oxygen atom by cleavage between Y- and –O-CTX, or to allow a carbocation by cleavage between Y-O- and –CTX;

with the possible presence of one or several reaction additives to form said sidechain-bearing cephalotaxane and/or a salt thereof.

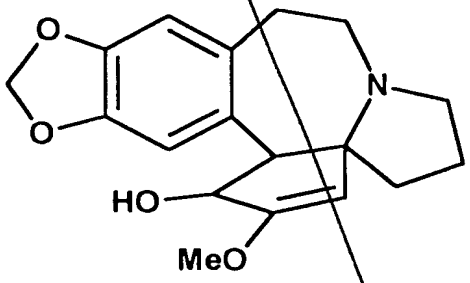
2. The process according to claim 1, wherein Z is an oxygen atom and the cephalotaxane H-O-CTX is a cephalotaxine of the following formula, or a salt

2. The process according to claim 1, wherein Z is an oxygen atom and the cephalotaxane H-O-CTX is a cephalotaxine of the following formula, or a salt thereof:



where R^1, R^2, R^3 and R^4 are independently hydrogen, hydroxyl group or alkoxide.

3. The process according to claim 2, wherein said cephalotaxane H-O-CTX is cephalotaxine, or a salt thereof, where R^1 is hydroxyl, R^2 is methoxyl, R^3 and R^4 are hydrogen.



4. The process according to ~~anyone of claims 1 to 3~~ claim 1, wherein R^5 is hydrogen.

5. The process according to ~~anyone of claims 1 to 3~~ claim 1, wherein R^5 is $-CH_2$-CO-O-Me.

6. The process according to ~~anyone of claims 1 to 5~~ claim 1, wherein n = 1 to 4, R^6 and R^8 are methyl.

7. The process according to ~~anyone of claims 1 to 5~~ claim 1, wherein n = 1 or 2, R^6 is phenyl and R^8 is hydrogen.

8. The process according to claim ~~1~~ wherein, R^5 is $-CH_2$-CO-O-Me, said cephalotaxane is the former of claim 3, n = 0, Z is a nitrogen atom and R^8 is hydrogen.

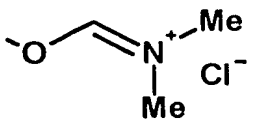
9. The process according to ~~anyone of claims 1 to 8~~ claim 1, wherein A is Ω-CO-O-radical ~~where Ω is as defined according to claim1~~.

10. The process according to ~~anyone of claims 1 to 8~~ claim 1, wherein A is halide.

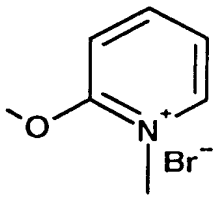
11. The process according to ~~anyone of claims 1 to 8~~ claim 1, wherein A is a radical of compound Ω-CO-A having the ability to generate cleavage of the bond between carbonyl group and substituent A of Ω-CO-A to provide Ω-$CO^{\bullet}$ and $A^{\bullet}$

12. The process according to ~~anyone of claims 1 to 8~~ claim 1, wherein A is a radical selected from substituents:

méthoxyformyloxy of formula MeOCOO-,
trifluoroacétyloxy of formula CF_3COO-,
alkylsulfonoxy of formula RSO_3-,
phosphoxy of formula $(RO)_2PO$-,
halophosphoxy of formula ROP(Cl)O-,
trialkylsilyloxy of formula R_3SiO-,
diméthyl-formamidinium chloride of formula:



or acyloxy-pyridinium bromide of formula:

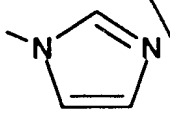


formulas wherein R is alkyl.

13. The process according to ~~anyone of claims 1 to 8~~ claim 1, wherein A is 2,4,6-trichlorobenzoyloxy radical

14. The process according to claim 13, wherein reagent of formula Ω-CO-A, A is 2,4,6-trichlorobenzoyloxy radical, is obtained by contacting an acid Ω-CO-OH, as defined according to claim 1, with 2,4,6-trichlorobenzoyl chloride in presence of one or more O-acylation additives.

15. The process according to ~~anyone of claims 1 to 8~~ claim 1, wherein radical A is corresponding to the following formula:



16. The process according to claim 15, wherein reagent of formula Ω-CO-A is obtained by contacting an acid Ω-CO-OH, ~~as defined according to claim 1~~, with carbonyl-diimidazole in presence of a strong base.

17. The process according to claim 16, wherein strong base is an alkoxide.

18. The process according to ~~previous claims~~ claim 1, wherein the coupling additive is a substituted carbodiimide and/or a basic additive ~~such as tertiary amine for example~~.

19. The process according to claim 18, wherein the substituted carbodiimide is selected from cyclohexylcarbodiimide (DCC), 1,3-diisopropylcarbodiimide (DIC) and chlorhydrate of 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide.

20. The process according to ~~anyone of previous claims,~~ claim 1 wherein cephalotaxine alcoxide ~~is corresponding~~ corresponds to the following formula:

M-O-CTX,

~~where M and CTX are as defined according to claim 1,~~

is obtained by contacting a cephalotaxine of the following formula:

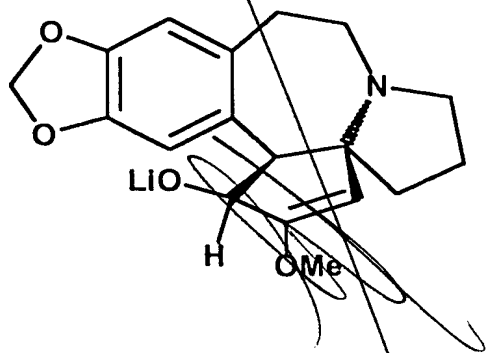
H-O-CTX

~~where CTX is as defined according to claim 1~~

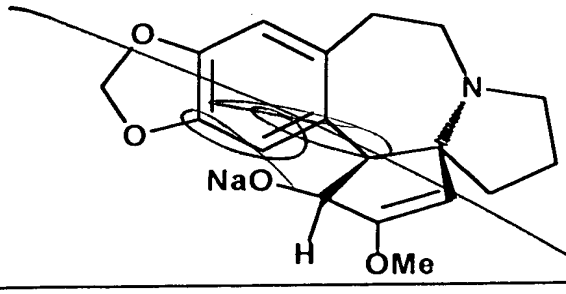
with metal ~~himself~~, an amidure, a metallic hydride or an alkyl-metal.

21. The process according to anyone of claims 1 to 20, wherein M is alkaline metal such as lithium, potassium or sodium.

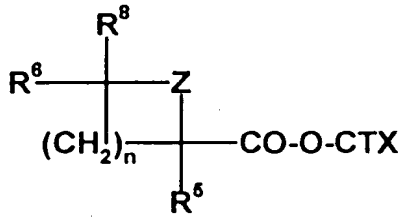
22. The lithium alcoxide of cephalotaxine ~~is~~ corresponding to the following formula:



23. The sodium alcoxide of cephalotaxine ~~is~~ corresponding to the following formula:



24. A sidechain-bearing cephalotaxane corresponding to the following formula and/or a salt thereof:



where

n is included between 0 and 8;

Z is oxygen, nitrogen or sulfur heteroatom;

R^5, R^6 and R^8 are independently

hydrogen;

hydrocarbon radical, saturated, insaturated or aromatic, linear or ramified and/or cyclic, especially alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heterocycloalkyl, of said radical including or not heteroatom(s);

oxygen ether bearing one of the former radicals;

CTX is as defined according to anyone of claims 1 to 3;

except for compounds where Z is oxygen atom and,

1°) n = 2 or 3, and simultaneously $R^6 = R^8$ = methyl and R^5 = OMe or hydroxyl,

1°) n = 2 and simultaneously $R^6 = R^8$ = methyl and R^5 = OMe or hydroxyl;

3°) n = 3 and simultaneously R^6 is hydroxyl, when R^8 is méthyl and R^5 is $-CH_2CO_2CH_3$ radical.

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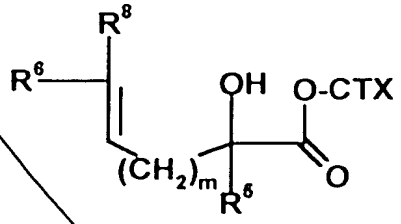
25. A sidechain-bearing cephalotaxane corresponding to the following formula and/or a salt thereof:



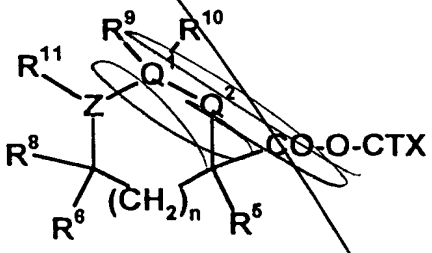
where

m, R^5, R^6 and R^8 are as defined according to claim 1, and CTX is as defined according to anyone of claims 1 to 3,

Except compound where m = 2, $R^5 = CH_2CO_2CH_3$, $R^6 = R^8$ = methyl and CTX is as defined according to claim 3.

26. The cephalotaxane according to claim 25, wherein R^5 is $-CH_2-CO-O-CH_3$ radical.

27. A sidechain-bearing cephalotaxane corresponding to the following formula and/or a salt thereof:



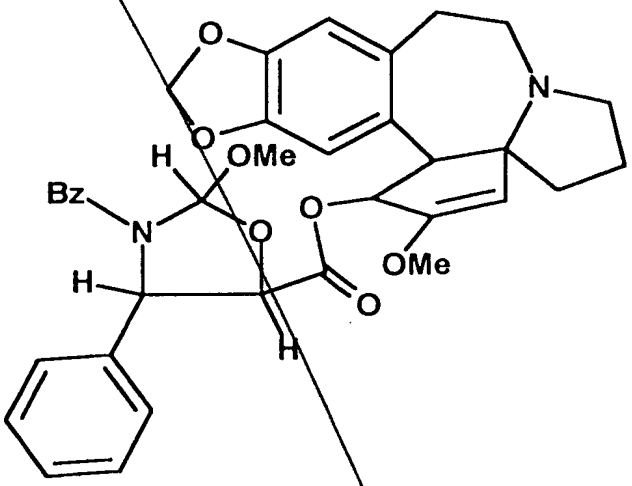
where n, Z, Q^1, Q^2, R^5, R^6, R^8, R^9, R^{10} and R^{11} are as defined according to claim 1, and CTX is ~~as~~ defined according to ~~anyone of claims 1 to 3,~~ claim 1

28. The cephalotaxane according to claim 27, wherein Q^2 is oxygen atom.

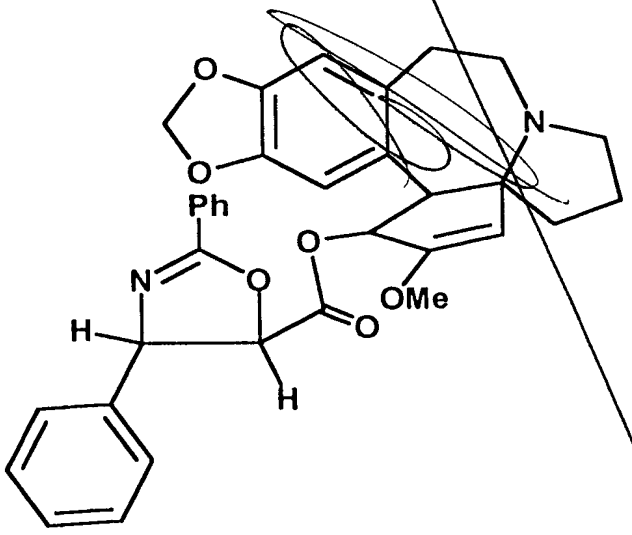
29. The cephalotaxane according to claim 28, wherein Z is nitrogen atom.

30. The cephalotaxane according to claim 29, wherein n =0.

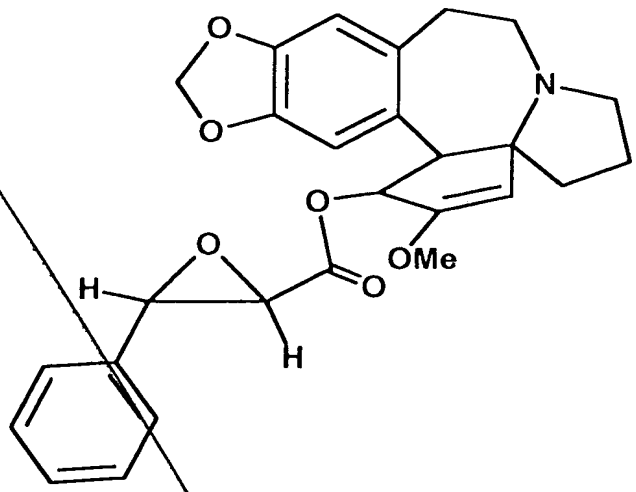
31. The sidechain-bearing cephalotaxane corresponding to the following formula:



32. The sidechain-bearing cephalotaxane corresponding to the following formula:

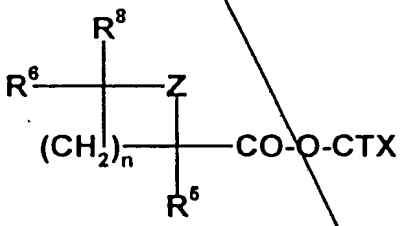


33. The sidechain-bearing cephalotaxane corresponding to the following formula:



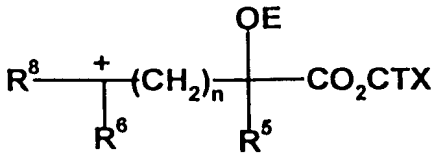
34. The process according to ~~anyone of claims 1 to 21~~ claim 1, wherein

- when the cyclic side-chain of sidechain-bearing cephalotaxane, and/or a salt thereof, of the following formula:



where n, R^5, R^6, R^8, CTX and Z are as defined according to claim 1;

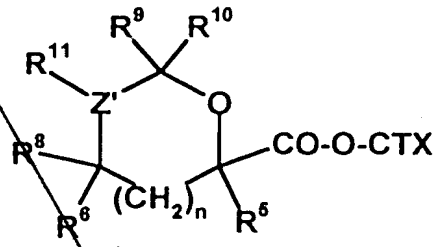
the said chain is open with an agent and/or a protonic or not protonic electrophilic radical E in aqueous or not aqueous medium, to provide an intermediate compound of the following formula:



where n, CTX, R^5, R^6 and R^8 are as defined above, E is either hydrogen or the provisionally or definitively fixed eletrophilic radical;

the aforementioned intermediate compound may be attacked with an agent or a nucleophilic radical Z', deliberately added or possibly present in the medium, and

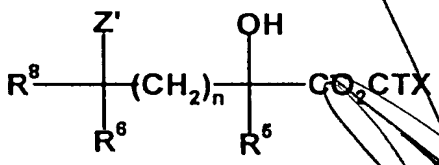
- when the cyclic side-chain of sidechain-bearing cephalotaxane, and/or a salt thereof, of the following formula:



where n, R^5, R^6, R^8, R^9, R^{10} and R^{11} are as defined according to claim 1, and Z' is an heteroatom;

the said chain is open by hydrolysis or carefully solvolysis with possibly presence of activation and/or opening additive;

- to provide an open sidechain-bearing cephalotaxane of the following formula:



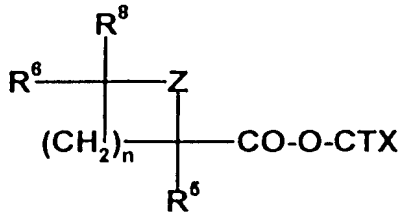
where n, CTX, R^5, R^6 and R^8 are as defined according to claim 1;

Z' is:

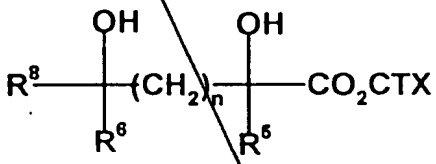
- either an halogen or an heteroatom bearing a hydrogen or a radical R^{11} such as defined accordint to claim 1;
- or an hydrogen, hydrocarbon radical, the said optionally radical bearing ~~or not~~ heteroatom(s), saturated, ~~insaturated~~ unsaturated or aromatic, linear or ~~ramified~~ branched and/or cyclic, ~~especially alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, or~~

~~heterocycloalkyl~~.

35. The process according to the claim ~~34~~ wherein the cyclic side-chain of sidechain-bearing cephalotaxane, and/or a salt thereof, of the following formula:



where n, R^8, R^6, R^5, CTX and Z are defined according to the claim 1, the said chain is open by treatment with a solution of hydrobromic acid in acetic acid, in an halogenated solvent, ~~preferably dichloromethane~~, followed by *in situ* hydrolysis to provide, without isolation of the intermediate, a sidechain-bearing cephalotaxane of the following formula:



~~where n, CTX, R^5, R^6 et R^8 are defined according to claim 1~~.

36. The process according to ~~anyone of claims 1 to 21 and claim 34~~, wherein acids are corresponding to the following formula :

Ω-CO-OH

~~where Ω radical is as defined according to claim 1~~,

the said formula equivalent to racemic mixture containing compounds of the formulas (+)-Ω-CO-OH and (-)-Ω-CO-OH ~~such as~~ (+)-Ω-CO-OH represents its dextrogyre enantiomer and (-)-Ω-CO-OH represent its levogyre enantiomer.

were obtained

a) by contacting of said racemic mixture or one of ~~its~~ activated ~~form~~ of the

formula

$$\Omega\text{-CO-A}$$

which is as defined according to claim 1;
the said racemic mixture or said activated form generating respectively:

- either an anion corresponding to the formula **(Ω-CO-O)$^-$**;
- or a cation corresponding to the formula **(Ω-CO)$^+$**;

with a pure enantiomeric form of chiral entity, said "resolution agent" symbolized by Δ^* (delta stella), having the ability to form:

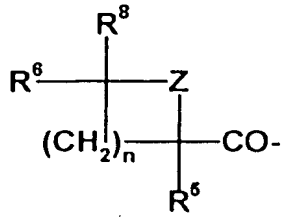
- either a stable combination, by covalent bonding;
- or an easily reversible labil combination, by hydrogen bonding or by hydrophobic interaction;
- or intermediate lability bonding by electrostatic interaction;

to provide a diastereomeric mixture of Ω-CO-O-Δ^* and de Ω-CO-Δ^*;

b) then by physical separation of the mixture of two diastereomers or two complex compounds or more generally of two new entities physically and/or chemically different then obtained;

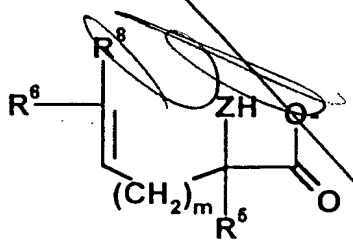
c) then by regeneration and finally separation of each one of enantiomers of the generic formula Ω^*-CO-OH,
where Ω^* («oméga stella») represents the generic symbol of the same chiral radical in the either one or the other pure enantiomeric forms corresponding to the following formulas **(+)-Ω-CO-OH and (-)-Ω-CO-OH** which are as defined above.

37. The process according to claim 36, wherein Ω-CO- is a radical corresponding to the following formula:



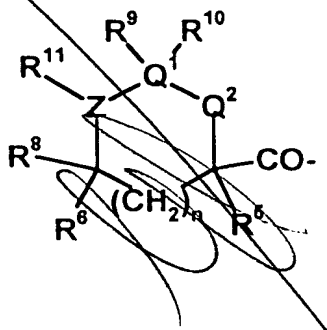
~~where n, Z, R^6, R^8, and R^5 are as defined according to claim 1.~~

38. The process according to claim 36, wherein Ω-CO- is a radical corresponding to the following formula:



~~where m, Z, R^6, R^8, and R^5 are as defined according to claim 1.~~

39. The process according to claim 36, wherein Ω-CO- is a radical corresponding to the following formula:



~~where n, R^5, R^6, R^8, Z, Q^2, Q^1, R^9, R^{10} and R^{11} are as defined according to claim 1.~~

40. The process according to ~~anyone of claims 36 to 39~~, wherein the stable combination is represented by an ester of the following formula **Ω-CO-O-Δ*** ~~such as Ω and Δ* are as defined according to claim 36~~, ~~the~~ said stable combination is obtained by contacting acid with a chiral alcohol corresponding to the formula **HO-Δ*** ~~such as Δ* is as defined according to claim 36, according the process of the claim 1~~.

41. The process according to claim 36 ~~anyone of claims 36 to 39~~, wherein the stable combination is represented by an amide corresponding to the either one or the other formulas **Ω-CO-NH-Δ*** **or Ω-CO-N-Δ*** ~~such as Ω and Δ* are as defined according to claim 36~~, ~~the~~ said stable combination is obtained by contacting acid with primary or secondary chiral amine corresponding to formulas **H_2N-Δ*** **or NN=Δ*** ~~such as Δ* is as defined according to claim 36, according the process of the claim 1~~.

42. The process according to claim 36 ~~anyone of claims 36 to 39~~, wherein the stable combination is represented by an thioester of the following formula **Ω-CO-S-Δ*** ~~such as Ω and Δ* are as defined according to claim 36~~, ~~the~~ said stable combination is obtained by contacting acid with a chiral thiol corresponding to the formula **HS-Δ*** ~~such as Δ* is as defined according to claim 36, according the process of the claim 1~~.

43. The process according to claim 36 ~~anyone of claims 36 to 39~~, wherein the ionic combination is represented by a salt ~~just~~ prepared by contacting of acid with a chiral amine corresponding to one of the ~~the either one or the other of the three~~ an following formulas:

Ω-CO-O$^-$ [NH-Δ*]$^+$

Ω-CO-O$^-$ [NH_2-Δ*]$^+$

Ω-CO-O$^-$ [NH_3-Δ*]$^+$

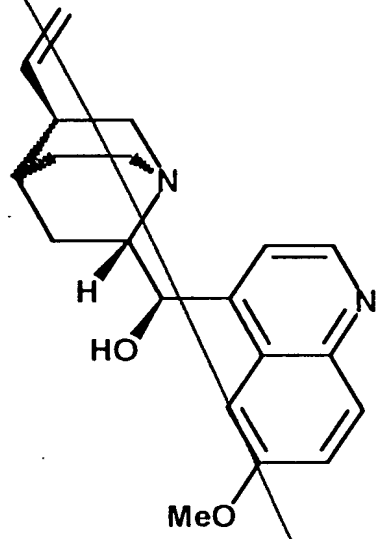
~~where Ω and Δ* are as defined according to claim 36~~.

44. The process according to claim 36 ~~anyone of claims 36 to 39~~, wherein the bringing

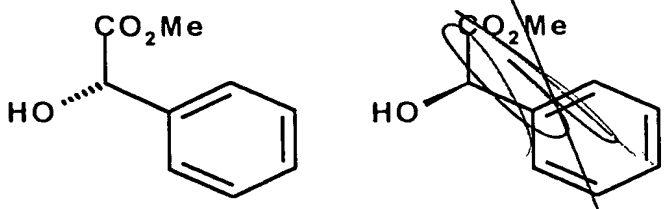
into play of a ~~labil~~ labile bonding based combination is achieved in the form of chromatography with the help of a chiral stationary phase.

45. The process according to ~~anyone of claims 36 to 39~~ claim 36, wherein the bringing into play of an interatomic or intermolecular ~~labil~~ labile bonding based combination, within crystalline latice, is achieved in the form of fractionated crystallization initiated by a chiral precursor.

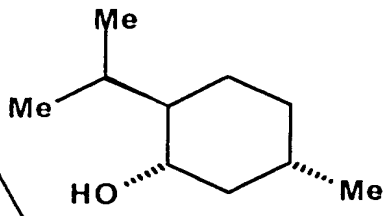
46. The process according to claim 40, wherein chiral alcohol HO-Δ* is (-)-quinine corresponding to the following formula:

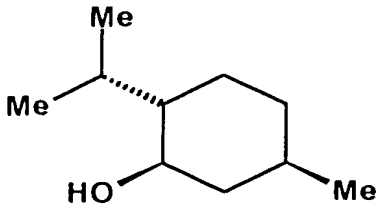


47. The process according to claim 40, wherein chiral alcohol HO-Δ* is (-)- or (+)-methyl mandelate corresponding to the following formulas:

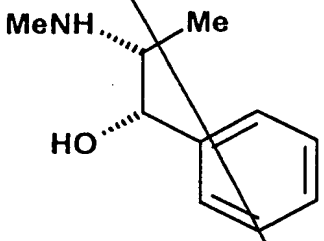


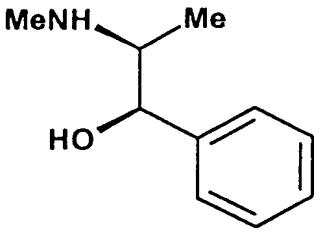
48. The process according to claim 40, wherein chiral alcohol HO-Δ* is (-)- or (+)-menthol corresponding to the following formulas:



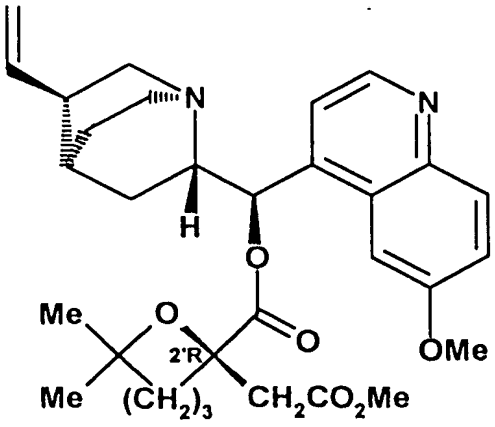


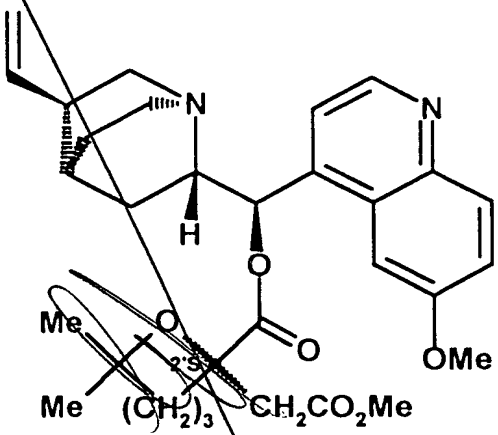
49. The process according to claim 43, wherein chiral amine H_2N-Δ* is (-)- or (+)-ephedrine corresponding to the following formulas:



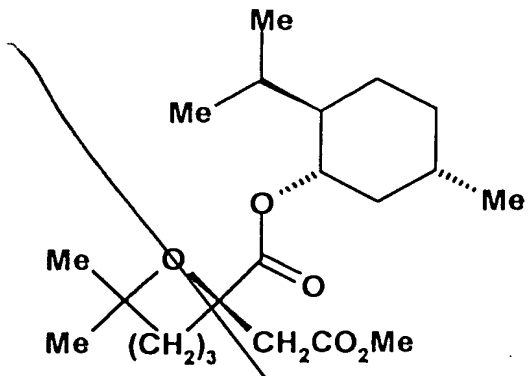


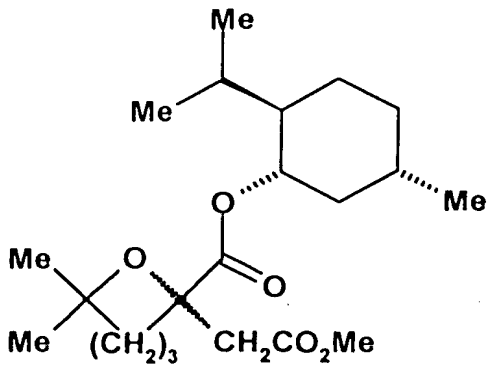
50. The (-)-quinidyl (2'R)-(-)-anhydro-homoharringtonate and the (-)-quinidyl (2'S)-(-)-anhydro-homoharringtonate corresponding respectively to the two following formulas:



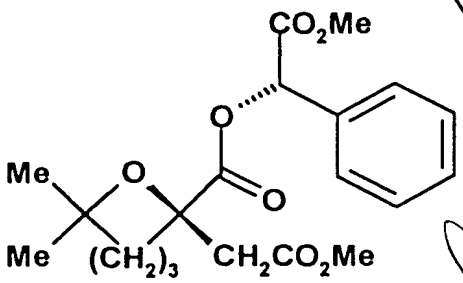


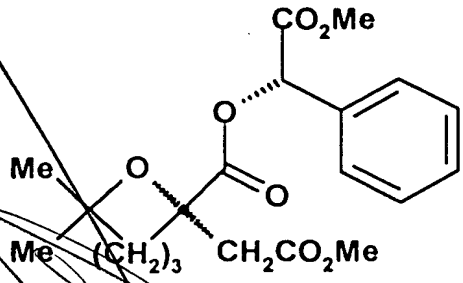
51. The (-)-menthyl (2'R)-(-)-anhydro-homoharringtonate and the (-)-menthyl (2'S)-(-)-anhydro-homoharringtonate corresponding respectively to the two following formulas:



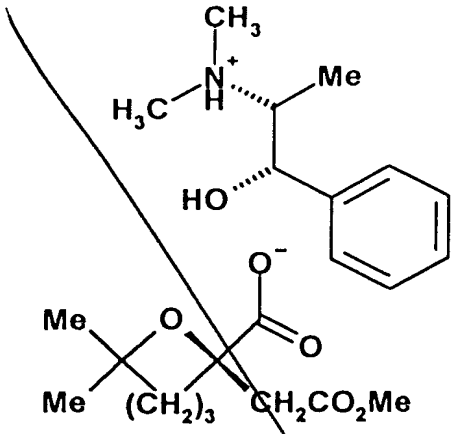


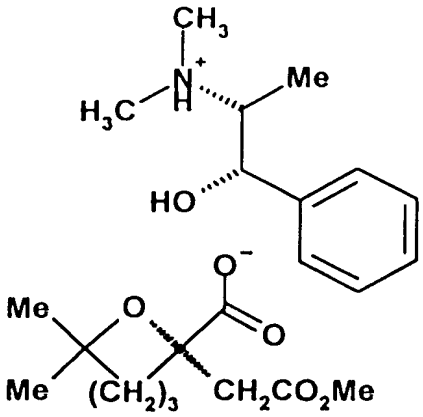
52. The (-)-methylmandelyl (2'R)-(-)-anhydro-homoharringtonate and the (-)-methylmandelyl (2'S)-(-)-anhydro-homoharringtonate corresponding respectively to the two following formulas:





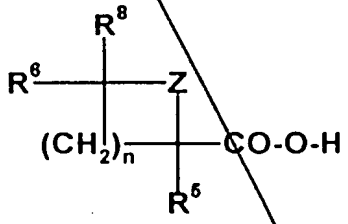
53. The (-)-ephedrinium (2'R)-(-)-anhydro-homoharringtonate and the (-)-ephedrinium (2'S)-(-)-anhydro-homoharringtonate corresponding respectively to the two following formulas:





54. The process according to ~~anyone of claims 1 to 21 and 34 to 49~~ claim 1, wherein the carboxylic acid is:

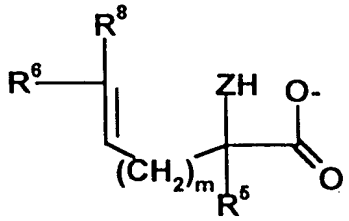
- either the tertiary heterocycloalcane carboxylic acid corresponding to the following formula:



where n, Z, R^5, R^6 and R^8 are as defined according to claim 1.

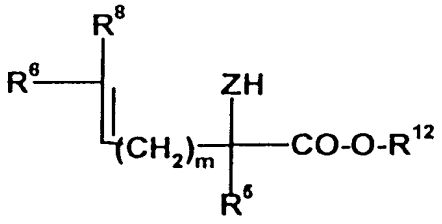
the said acid is obtained by treatment in aprotic or protic solvant, eventually in the presence of cyclization additive and/or dehydrating agent, the said treatment eventually supported with physical carrying of the water formed;

- or open tertiary ethylenic acid corresponding to the following formula:



where m, Z, R^5, R^6 and R^8 are as defined according to claim 1.

- or open tertiary ethylenic acid corresponding to the following formula:



where m ~~is included between 1 and 8~~, Z, R^5, R^6 and R^8 are as defined according to claim 1, R^{12}, is not a CTX radical according to claim 1, represents R^5 and/or a protective group of acids and/or a chiral group;
then R^{12} is removed later, either just by saponification, or by hydrogenolysis, or ~~more generally by the method of the state of art to~~ remove protective groups of acids.

55. The process according to claim 54, wherein in the absence of cyclization additive, the reaction of cyclization ~~just take place~~ by heating.

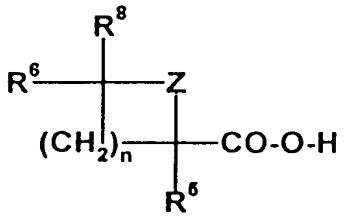
56. The process according to claim 54, wherein the cyclization additive is a protic acid or an aprotic acid, included in immobilized form.

57. The process according to claim 54, wherein the acid is sulfonic acid or formic acid.

58. The process according to ~~anyone of claims 54 to 57~~, wherein Z is an oxygen atom.

59. The tertiary heterocycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:

Sub a4 cont.?



where n is included between 1 and 8, Z, R^5, R^6 and R^8 are as defined according to claim 1, and R^5 is not hydrogen;

except for compounds where Z is oxygen atom and,

1°) n = 0 and R^5 is not $-CH_2CO_2H$ or $-CH_2CO_2CH_3$ radical;

2°) n = 0 and R^5 is $-CH_2CO_2H$ or $-CH_2CO_2CH_3$ radical, and R^6 = R^8 = methyl or $-CH_2CO_2H$ or $-CH_2CO_2CH_3$ radical;

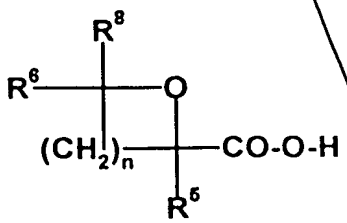
3°) n = 2 and simultaneously R^6 = R^8 = methyl, and R^5 = OMe or hydroxyl ;

4°) n = 2 and simultaneously R^6 = R^8 = methyl, and R^5 is $-CH_2CO_2H$ or $-CH_2CO_2CH_3$ radical or methyl;

5°) n = 3 and simultaneously R^6 is hydroxyl, and R^8 is methyl, and R^5 is $-CH_2CO_2CH_3$ radical;

6°) n = 3 and simultaneously R^6 = R^8 = methyl and R^5 = OH or methyl or ethyl.

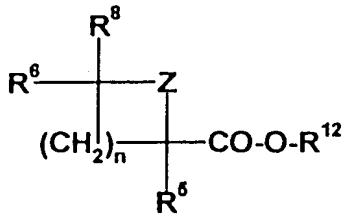
60. The tertiary oxacycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



where n is included between 0 and 8, R^5, R^6 and R^8 are as defined according to claim 59, but are not hydrogen simultaneously.

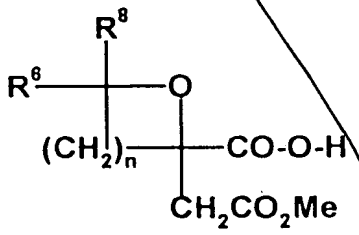
Sub a4 cont.

61. The tertiary heterocycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



where n is included between 0 and 8, Z, R^5, R^6 and R^8 are as defined according to claim 59, and R^5 is not hydrogen, and R^{12} is defined according to claim 54.

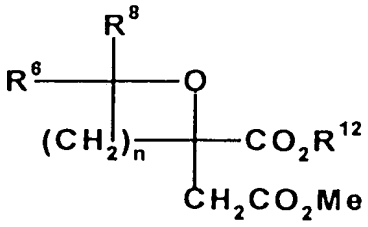
62. The tertiary oxacycloalcane carboxylic hemiester, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



where n is included between 0 and 8, R^6 and R^8 are as defined according to claim 59.

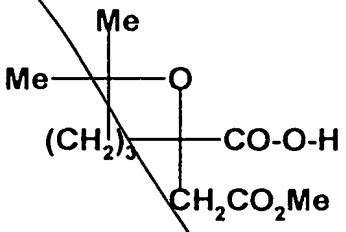
63. The tertiary oxacycloalcane carboxylic hemiester, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:

Sub a4 cont 7

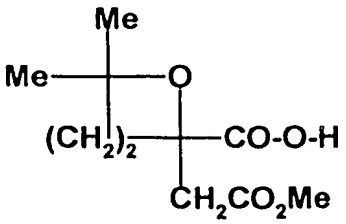


where n is included between 0 and 8, R^6 and R^8 are as defined according to claim ~~59~~, R^{12} is defined according to claim 54.

64. The tertiary oxacycloalcane carboxylic hemiester or anhydro-homoharringtonic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



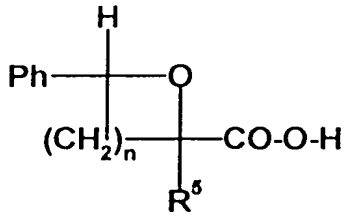
65. The tertiary oxacycloalcane carboxylic hemiester or anhydro-harringtonic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



66. The tertiary oxacycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition,

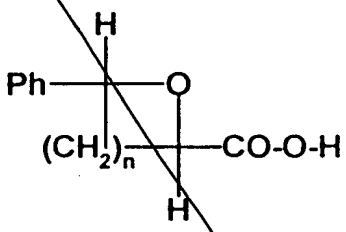
Sub 7 a4 cont.

corresponding to the following formula:



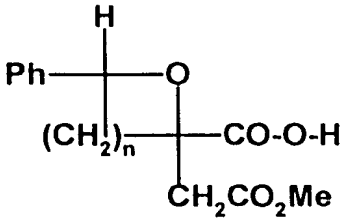
where n is included between 0 and 8, R^5 is as defined according to claim 59.

67. The tertiary oxacycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



where n is included between 1 and 8.

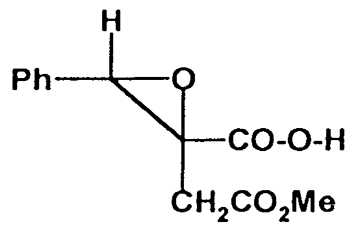
68. The tertiary oxacycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



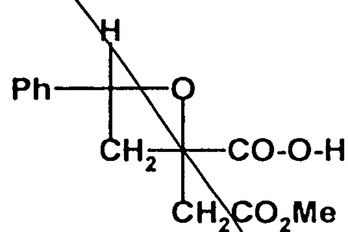
where n is included between 0 and 8.

69. The tertiary oxacycloalcane carboxylic acid or oxanhydroneoharringtonic

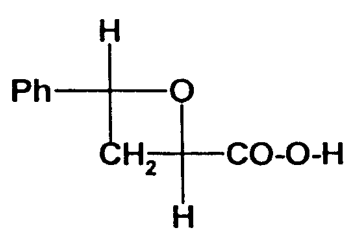
acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



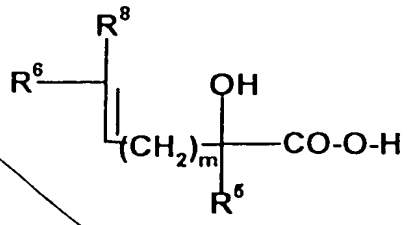
70. The tertiary oxacycloalcane carboxylic acid or oxanhydroneohomoharringtonic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



71. The tertiary oxacycloalcane carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:

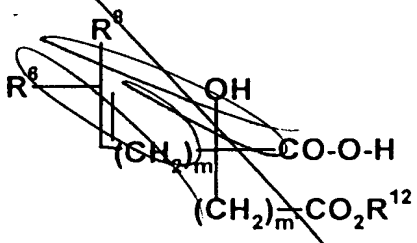


72. The tertiary alkene carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



where m is included between 1 and 8, R^6 and R^8 are as defined according to claim ~~1~~, but are not hydrogen simultaneously, and R^5 is not hydrogen or heteroatom.

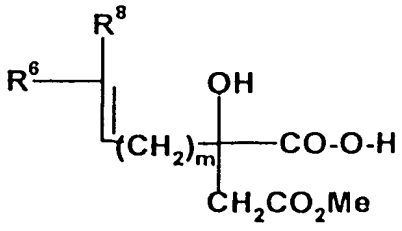
73. The tertiary ~~a~~lkene carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, according to claim 54 corresponding to the following formula:



~~where m is included between 1 and 8, m' is included between 1 to 8, R^6 and R^8 are as defined according to claim 1 and and R^{12} is defined according to claim 54.~~

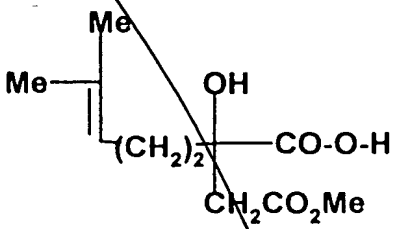
74. The tertiary alkene carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:

Sub a5 cont.

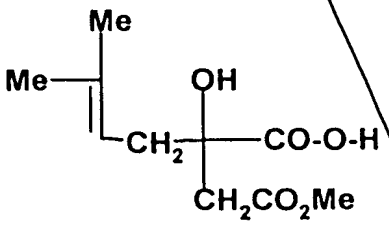


where m is included between 1 and 8, R^6 and R^8 are as defined according to claim 1 but are not hydrogen.

75. The tertiary alkene carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:

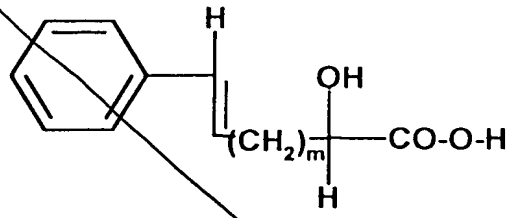


76. The tertiary alkene carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:



77. The tertiary alkene carboxylic acid, included its salts and each one of its pure enantiomeric forms or in racemic mixture or in variable composition, corresponding to the following formula:

Sub ascent.



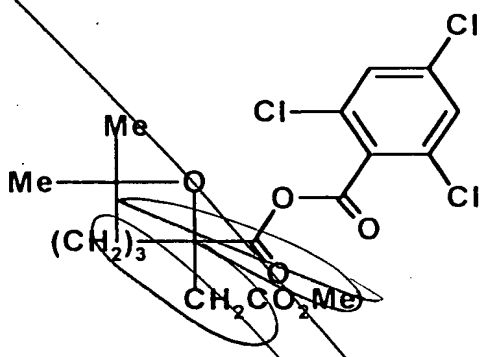
where m is included between 1 to 8.

78. The compound according to claim 77, where m = 1.

79. The anhydrides of acid according to anyone of claims 58 to 70, of the general formula **Ω-CO-O-CO-Ω** where Ω is as defined according to claim 1.

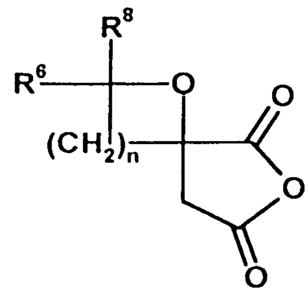
80. The mixed anhydrides of acid according to anyone of claims 58 to 70, of the general formula **Ω-CO-A** where A is as defined according to anyone of claims 12, 13 or 15.

81. The mixed anhydride corresponding to the following formula:



claim 58

82. The acid chlorides according to ~~anyone of claims 58 to 70;~~ corresponding to the ~~general~~ formula **Ω-CO-X**, where **X** is halogen.

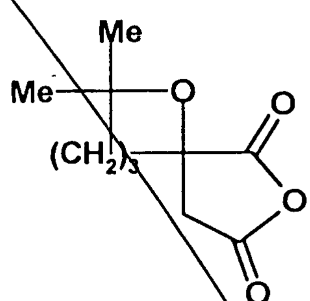


Sub7 a7

83. The cyclic anhydrides corresponding to the following formula:

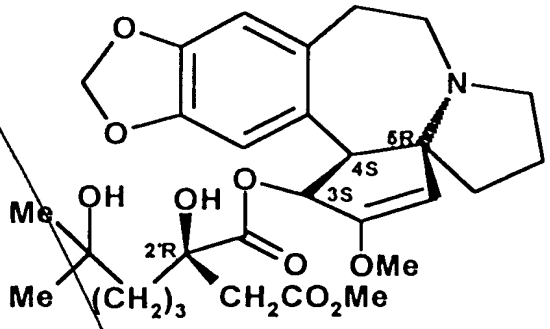
where n, R^6 and R^8 are as defined according to claim 1.

84. The cyclic anhydride corresponding to the following formula:



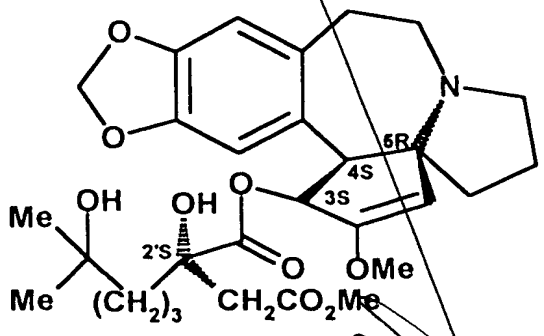
85. The process according to claim 1 ~~anyone of claims 1 to 21 and 34 to 49~~ where the sidechain-bearing cephalotaxane was purified like a salt by chromatography using a reversed-phase like stationary phase, and a mobile phase without organic solvent like a solution adjusted to a pH 2 to 4.5 with a buffer prepared with an acid and an alkaline or ammonium salt and one or several additive like attenuator of silanol effect, the said cephalotaxine salt was generated from mineral acid under the form of chlorohydrate, sulfate, phosphate, nitrate, perchlorate, or from organic acid under the form of tartrate, malate, citrate or lactate.

86. The process according to ~~anyone of claims 1 to 21 and 34 to 49~~ claim 1 comprising a step of chromatographic purification of a natural or semi-synthetic or synthetic homoharringtonine ~~as a pharmaceutical use~~ corresponding to the following formula:



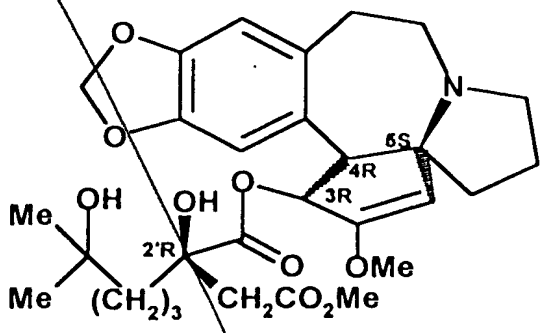
to remove the undesired related impurity ~~named~~ 2'-épi-homoharringtonine resulting:

a) either from a semi-synthetic process with introduction of a synthetic homoharringtonic acid of inadequate enantiomeric purity, the generated impurity showing the absolute configuration corresponding to the following formula:



b) or from the biosynthetic process in the plant, where a cephalotaxine with inadequate enantiomeric purity was introduced, or in the form of artefact by partial racemization of the cephalotaxine moiety, the generated impurity showing strictly identical chromatographic properties with a non-chiral system,

with an absolute configuration opposite to the one above (enantiomer) and corresponding to the following formula:



using
~~especially making use of~~ one of the following chromatographic systems:

A) Stationary phase:

alkyl- or phenyl- or alkylphenyl- ou phenylalkyl-silane, ~~preferably *n*-octadecylsilane,~~

B) Mobile phase:

water-tetrahydrofurane, water-methanol, water-acetonitrile or buffer pH 2 to 6.5 in replacement of water, or all other mobile phase with equivalent selectivity,

87. The process of purification and chromatographic control according to the claim 86 of a natural or semi-synthetic or synthetic homoharringtonine, allowing to offset the double insufficiency of enantiomeric purity of the half-precursors, both on the sidechain precursor (said homoharringtonic acid) and cephalotaxine, the two said-precursors are each independently generated by total synthesis or semi-synthetic process or natural process within of the plant (biosynthesis), in fact the withdrawal of the non natural enantiomer of homoharrintonine showing an opposite absolute configuration, by using a chiral stationary phase with preparative scale.